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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/7349, 177	12/02/94	GREY	H 14137-58-4

020350 HM11/1109
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EXAMINER	
SCHWADRON, R	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/09/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/349,177	Applicant(s) Grey et al.
	Examiner Ron Schwadron, Ph.D.	Group Art Unit 1644

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 19-55 is/are pending in the application.

Of the above, claim(s) 19-36 and 38-55 is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 37 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

15. Applicant's election of the species wherein the motif has amino acid L at position two and I at the C terminus in Paper No. 24 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

16. Claims 38-47 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected inventions. Election was made **without** traverse in Paper No. 24. As enunciated in paragraph 16 of the previous Office Action, claims 48-55 were previously withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species (as per the election of species requirement enunciated in the Office Action mailed 2/6/96 and Office Action mailed 12/23/96), the requirement having been traversed in Paper No. 5 and 7.

17. Regarding claim 37, claim 37 is under consideration only in so far as it reads on the elected species of a peptide of 9 amino acids. Applicant elected the species of a nine amino acid peptide in paper no. 5. The species wherein the motif has L at position two and I at the C terminus is only present in a 9-mer peptide in claim 37. Claims 19-36 were withdrawn from consideration as being directed to a non-elected invention (see 37 CFR 1.142(b) and MPEP § 821.03) in paragraph 15 of the previous Office Action. Regarding applicants comments in pages 2-4 of the amendment file 8/14/98, the following comments are made. Claims 19-36 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Original claims 1-10 (and claims 37-55) are drawn to a composition, classified in Class 530, subclass 350 and Class 514, subclass 15. Claims 19-36 are drawn to a method of inducing a CTL response in a patient, classified in Class 435, subclass 2 and Class 424, subclass 184.1. The inventions of claims 37-55 and 19-36 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product can be used to stimulate T cell responses

from normal individuals (eg. nonpatients) or used in in vitro assays to detect CTL. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 19-36 were withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

The MPEP, section 803 (July 1998) states:

CRITERIA FOR RESTRICTION BETWEEN PATENTABLY DISTINCT INVENTIONS

There are two criteria for a proper requirement for restriction between patentably distinct inventions:

(1) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 - § 806.05(I)); and

(2) There must be a serious burden on the examiner if restriction is not required (see MPEP § 803.02 § 806.04(a) - (j), § 808.01(a) and § 808.02).

The instant restriction requirement has explained why the claims under discussion are independent or distinct. The M.P.E.P. § 803 (July 1998, page 800-4) states that:

*For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search.*

The restriction requirement enunciated in the Office Action mailed 5/11/98 meets this criterion and therefore establishes that serious burden is placed on the Examiner by the searching of additional Groups. Regarding In re Pleuddemann, In re Pleuddemann deals with issues related to obviousness and prior art. It is not related to PTO restriction requirement policy and does not address PTO restriction requirement policy. Applicant is referred to the MPEP Chapter 800 for a complete description and explanation of PTO restriction requirement policy.

18. Claim 37 is under consideration.

19. Applicants need to update the status of all US patent applications listed in the specification (eg. abandoned, etc) including those disclosed on page 1.

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the peptide of claim 37 for the following reasons.

A) There is no support in the specification as originally filed for a 9-mer peptide with the motif recited in claim 37. Original claims 1-10 recite motifs for 9-mer peptides. The motif recited in claim 37 is not the motif recited in original claims 1-10 for 9-mer peptides. Claim 37 recites a motif that applies to a 9-mer peptide, wherein said motif is not disclosed in original claims 1-10 or the specification. There is no disclosure in the specification or original claims 1-10 of a 9mer peptide containing a L,M,I,V,A or T at the second position and V,I,L,A or M at the c-terminal. While original claim 11 encompasses such a motif, original claim 11 is drawn to a 10-mer, not a 9-mer peptide. There is no support in the specification as originally filed for the claimed invention (it constitutes new matter).

B) There is no support in the specification as originally filed for recitation of "wherein the immunogenic peptide binds the HLA-A.21 MHC product with a dissociation constant that is less than 100 times the dissociation constant of a peptide having a sequence FLPSDYFPSV" in the context recited in claim 37. There is no disclosure of the claimed composition in the original claims or specification. Regarding applicants comments in page 5 of the amendment filed 11/4/97, the following comments are made. While parent application 08/159,184, pages 38 and 39 disclose a binding assay using peptide FLPSDYFPSV, said pages of the specification do not disclose the composition recited in claim 37. Regarding Table 5 of parent application 08/159,184, said Table does not disclose the claimed invention. Regarding page 44 of parent application

08/159,184, said page does not disclose the claimed invention. There is no disclosure in parent application 08/159184 of a composition with the motif recited in claim 37, wherein the peptide is limited to peptides "wherein the immunogenic peptide binds the HLA-A.21 MHC product with a dissociation constant that is less than 100 times the dissociation constant of a peptide having a sequence FLPSDYFPSV". The particular passages of the specification and Table 5 of parent application 08/159184 to which applicant refers do not disclose the claimed invention. Said passages of the specification and Table 5 disclose an experimental assay and a particular set of experimental results, but do not disclose the claimed invention. Table 5 refers to experiments done using substitutions in a "9-mer prototype poly-A binder" (see page 39). This peptide and the substituted variants tested in Example 5 are not the claimed invention (eg. they are not the peptide motif recited in claim 37). There is no support in the specification as originally filed for the claimed invention (it constitutes new matter).

C) There is no support in the specification as originally filed for recitation of "where the immunogenic peptide is not ALWNLHGQA" in claim 37. The peptide ALWNLHGQA is not disclosed in the instant application or any application to which the instant application claims priority. There is also no disclosure in the specification as originally filed of the scope of the claimed invention (any peptide encompassed by the formula recited in the claim except ALWNLHGQA). Regarding applicants about In re Johnson and Farnham , In re Johnson and Farnham is not relevant to the issue under consideration because said case refers to a situation wherein generic claims were amended to exclude species that were disclosed in the specification of the application under consideration (see page 195 and 196). The peptide ALWNLHGQ is not disclosed in the instant application or parent applications. The MPEP section 2163.06 (July 1998, page 2100-143) states: *The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as - filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. In Ex parte Ohshiro , 14 USPQ2d 1750 (Bd. Pat. App. & Inter. 1989), the Board affirmed the rejection under 35 U.S.C. 112, first paragraph, of claims to an internal combustion engine which recited "at least one of said piston and said cylinder (head) having a recessed channel." The Board held that the application which disclosed a cylinder head with a recessed channel and a piston without a*

recessed channel did not specifically disclose the "species" of a channeled piston.

While this and other cases find that recitation of an undisclosed species may violate the description requirement, a change involving subgeneric terminology may or may not be acceptable. Applicant was not entitled to the benefit of a parent filing date when the claim was directed to a subgenus (a specified range of molecular weight ratios) where the parent application contained a generic disclosure and a specific example that fell within the recited range because the court held that subgenus range was not described in the parent application. In re Lukach , 442 F.2d 967, 169 USPQ 795 (CCPA 1971). On the other hand, in Ex parte Sorenson , 3 USPQ2d 1462 (Bd. Pat. App. & Inter. 1987), the subgeneric language of "aliphatic carboxylic acid" and "aryl carboxylic acid" did not violate the written description requirement because species falling within each subgenus were disclosed as well as the generic carboxylic acid. See also In re Smith , 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) ("Whatever may be the viability of an inductive - deductive approach to arriving at a claimed subgenus, it cannot be said that such a subgenus is necessarily described by a genus encompassing it and a species upon which it reads." (emphasis added)). Each case must be decided on its own facts in terms of what is reasonably communicated to those skilled in the art. In re Wilder , 736 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984).

There is no support in the specification as originally filed for the claimed invention (it constitutes new matter).

D) There is no support in the specification as originally filed for the recitation of "has about 9 or 10" in claim 37. Original claim 1 discloses that the immunogenic peptide "has 9 residues". There is no support in the specification as originally filed for the claimed invention (it constitutes new matter).

22. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Regarding applicants comments in the instant amendment the following comments are made. No rejection under 35 U.S.C. 101 is present in the instant Office Action. There are no claims presently under consideration drawn to in vivo methods of use or pharmaceutical compositions. The rejection under consideration is under 35 U.S.C. 112, first paragraph and addresses functional properties of the peptide recited in the claimed invention. The specification is not enabling for the claimed composition of peptides wherein said peptides are "immunogenic". The claimed invention recites that the peptide is "immunogenic". The specification discloses that an immunogenic peptide is "a peptide which comprises an allele-specific motif such that the peptide will bind an MHC molecule and induce a CTL response" (page 3, last paragraph, continued on page 4). The specification provides no evidence that the peptides recited in the claims are immunogenic. The specification provides no evidence that the binding data disclosed in the specification in Table 3 and 4 establishes that the peptides disclosed in said Tables are actually immunogenic (eg. capable of stimulating a T cell response). Celis et al. teach that in order to establish whether a peptide is immunogenic said peptide needs to be tested in assays that actually establish that a peptide is immunogenic (eg. CTL assay, etc.). Celis et al. teach that:

"In addition to MHC binding, other factors such as antigen processing, peptide transport and the composition of the T-cell receptor repertoire could determine whether any of these peptides can function as effective CTL antigens."

No such data is disclosed in the specification with regards to peptides that are disclosed in Tables 3 and 4 of the specification. Rammensee et al. teach that "MHC/peptide binding assays have a history of leading to obsolete results" (see page 182, first column). Rammensee et al. teach problems with interpreting data derived from said assays (see page 182, first column). It would require undue experimentation to determine which peptides encompassed by the formulas recited in the claims are actually immunogenic and which are not. Undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

While claim 37 recites functional parameters regarding the binding constant of the claimed peptide, it would require undue experimentation to determine which of the trillions of peptides encompassed by the claimed invention are "immunogenic" and which are not. It would require undue experimentation to determine which of the trillions of peptide recited in the claim did or

did not bind the HLA-A.21 MHC product with a dissociation constant that is less than 100 times the dissociation constant of a peptide having a sequence FLPSDYFPSV. Furthermore, even regarding peptides that bind the HLA-A.21 MHC product with a dissociation constant that is less than 100 times the dissociation constant of a peptide having a sequence FLPSDYFPSV, there is no evidence of record that said peptides would necessarily be "immunogenic" as the term is defined in the specification. The specification discloses that an immunogenic peptide is "a peptide which comprises an allele-specific motif such that the peptide will bind an MHC molecule and induce a CTL response". Celis et al. teach that in order to establish whether a peptide is immunogenic said peptide needs to be tested in assays that actually establish that a peptide is immunogenic (eg. CTL assay, etc.). Celis et al. teach that:

"In addition to MHC binding, other factors such as antigen processing, peptide transport and the composition of the T-cell receptor repertoire could determine whether any of these peptides can function as effective CTL antigens.".

No such data is disclosed in the specification with regards to peptides that are disclosed in Table 3 of the specification. Rammensee et al. teach that "MHC/peptide binding assays have a history of leading to obsolete results" (see page 182, first column). Rammensee et al. teach problems with interpreting data derived from said assays (see page 182, first column). Ochoa-Garay et al. teach that "In summary, the results in this report indicate that the immunogenicity of a peptide cannot always be predicted from its affinity for class I or the presence of class I binding motifs. In addition, our data show that variables such as CTL precursor frequency, peptide hydrophobicity and stability can influence the in vitro induction of CTL responses." (page 279, last sentence continued on page 280). Regarding Sette et al. (PNAS USA, 1989), said publication involves the testing of peptides *that were already known T cell epitopes* (eg. were known to be immunogenic before they were tested). Said publication does not establish that randomly picked peptides corresponding to a particular motif can be determined to be immunogenic based on in vitro MHC binding assays. Regarding applicants comments about a Schaeffer et al. publication, no such reference is of record on a PTO-892 or 1449 in the instant application and a copy of said reference has not been furnished so said reference was not considered. Regarding De Bruijn et al. (Eur. J. Immunol.), said reference does not disclose MHC class I binding motifs or the derivation of peptides based on MHC class I binding motifs. Regarding Pamer et al., said reference does not disclose that randomly picked peptides based on a motif bind a particular MHC class I allele and

that said peptides are also immunogenic. Said reference discloses that when peptides are derived from a known immunogenic protein, that one peptide so picked was immunogenic. It also discloses that even when a particular motif is applied to a protein sequence based on a known immunogenic peptide that 90 percent of the peptides picked were not immunogenic (see page 855). Thus, none of the aforementioned references demonstrate that MHC class I binding motifs can be used to predictably determine immunogenic peptides from a motif which encompasses trillions of peptides wherein a vast number of said peptides are not even found in any known protein sequence. Celis et al. teach that in order to establish whether a peptide is immunogenic said peptide needs to be tested in assays that actually establish that a peptide is immunogenic (eg. CTL assay, etc.). Celis et al. teach that:

“In addition to MHC binding, other factors such as antigen processing, peptide transport and the composition of the T-cell receptor repertoire could determine whether any of these peptides can function as effective CTL antigens.”. (see page 1430).

No such data is disclosed in the specification with regards to peptides that are disclosed in Table 3 of the specification. Regarding applicants comments about Celis et al. said reference is drawn to the use of MHC class I binding motif to attempt to determine immunogenic peptides based on the sequence of a known immunogen. There is no evidence supplied in Celis et al. that any peptide chosen from a known protein based on a MHC class I binding motif is immunogenic (as the term is defined in the specification) because the peptides disclosed in Celis et al. are not tested in CTL assays. Furthermore, Celis et al. discloses that “In addition to MHC binding, other factors such as antigen processing, peptide transport and the composition of the T-cell receptor repertoire could determine whether any of these peptides can function as effective CTL antigens.”. (see page 1430). Regarding applicants comments about inoperable embodiments, there is no disclosure in the specification as to what portion of the trillions of peptides recited in the claim would bind with the affinity recited in the claim and which are ultimately immunogenic. Rammensee et al. teach that “MHC/peptide binding assays have a history of leading to obsolete results” (see page 182, first column). Rammensee et al. teach problems with interpreting data derived from said assays (see page 182, first column). Ochoa-Garay et al. teach that “In summary, the results in this report indicate that the immunogenicity of a peptide cannot always be predicted from its affinity for class I or the presence of class I binding motifs. In addition, our data show that variables such as CTL precursor frequency, peptide hydrophobicity and stability can influence the in vitro induction of

CTL responses."(page 279, last sentence continued on page 280).

Karin et al. teach that amino acids in an MHC binding peptide that are not the amino acids which participate in MHC binding can have a profound effect on whether or not a peptide is immunogenic. The claimed invention recites a motif wherein residues not involved in MHC are not specified. Karin et al. teach that a single substitution in an amino acid, wherein said amino acid plays no role in MHC binding can completely abrogate the immunogenicity of an otherwise immunogenic peptide (see Summary and Table 1). Thus, Karin et al. establish that amino acids not recited in the claimed peptide (eg. amino acids not involved in MHC binding of a peptide) will play a pivotal role in determining whether the peptide recited in the claims is immunogenic. Karin et al. also establish that is unpredictable in the absence of empirical data whether a particular peptide which binds MHC will be immunogenic based on knowledge of whether the peptide has a particular MHC binding motif because amino acids outside of the MHC binding motif are a critical determining factor with regards to whether a particular peptide is immunogenic.

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25. Claim 37 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hunt et al.

Regarding priority for the claimed invention, for the same reasons that the claimed invention constitutes new matter (as elaborated in paragraph 21 of this Office Action), the claimed

invention is not entitled to priority to parent application 08/027146, because the instant invention is not disclosed in said application.

Hunt et al. teach the 9-mer peptide YLLPAIVHI (see Table 1). Hunt et al. teach a composition comprising said peptide (see Figure 3). Hunt et al. teach that said peptide binds to HLA-A2.1 (see page 1263, first column). The binding affinity and immunogenicity of said peptide are inherent properties of said peptide. Based on the binding shown in Figure 3, it appears that the peptide YLLPAIVHI binds to HLA A2.1 with high affinity (eg. it appears that it would have the dissociation constant recited in the claims). The dissociation constant and immunogenicity of the aforementioned peptide are an inherent property of said peptide. Therefore the claimed composition appears to be same or similar to the composition of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the composition of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

26. Claims 1-10 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Falk et al.

The claims read on a composition comprising and therefore encompass peptide mixtures containing the peptide recited in the claims. Falk et al. teach a mixture of peptides eluted from HLA-A2 cells (see page 292, second column, last paragraph and Table 4). Falk et al. teach that HLA-A2 presented peptides are nonamers (page 293). Thus, the peptides contained in the aforementioned composition are nonamers. In view of the fact that said mixture contains a vast variety of different HLA-A2 binding peptides and said peptides encompass the amino acid residues as per Table 4, it appears that the mixture of peptides eluted from HLA-A2 cells contains the claimed peptide. Therefore the claimed composition appears to be same or similar to the composition of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the composition of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

Regarding applicants arguments, the mixture of peptides eluted from HLA-A2.1 cells

disclosed in Falk et al. would contain the peptide recited in the claims because the motif recited in claim 37 is derived by analyzing peptides eluted from HLA-A2.1 positive cells (see specification, page 9). Thus, both the peptides disclosed in the prior art and the peptide recited in the claim are derived from HLA-A2.1 positive cells. It is an inherent property of the mixture disclosed by Falk et al. that it contains the peptide recited in the claim and the properties of the peptide are an inherent property of said peptide. Claim 37 reads on a composition comprising and therefore encompasses peptide mixtures containing the isolated peptide recited in the claims. Falk et al. teach a mixture of peptides eluted from HLA-A2 cells (see page 292, second column, last paragraph and Table 4). These peptides are isolated. Falk et al. teach that HLA-A2 presented peptides are nonamers (page 293). Thus, the peptides contained in the aforementioned composition are nonamers. In view of the fact that said mixture contains a vast variety of different HLA-A2 binding peptides and said peptides encompass the amino acid residues as per Table 4, it appears that the mixture of peptides eluted from HLA-A2 cells contains the claimed peptide.

27. Publications not considered on the PTO-1449 filed 7/7/97 were already of record on the PTO-892 mailed with Office Action mailed 12/23/96.

28. No claim is allowed.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-3014.

31. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ms Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.



RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644
November 7, 1998